PREVENTION AND TREATMENT

It is easy to understand that prevention of the conditions mentioned is only possible to a limited degree. And little can be said about their prevention and treatment that experienced trainers do not know. The theories merely support the practical rules of training which were found empirically.

To mention these briefly. The training work should be started with small demands and increased gradually. Sufficient rest periods must be interspersed. No effort in training should be carried to the point of complete muscular exhaustion. Once the muscles have reached a state of severe fatigue or strain, they should not be exercised until they have fully recuperated.

The process of recovery can be accelerated by the accepted methods known to stimulate the recuperation and circulation of the muscles, *i. e.*, heat in any form, and massage.

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THE OVARY OF THE RAT AFTER HYPOPHYSECTOMY

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MUCH former experimental work has shown that the functioning of the ovary depends upon the presence of the hypophysis and its hormones. In another paper of this series it will be shown that an excess of these hormones has a depressing effect upon the growth of follicles and the production of new germ cells. A further study of the hypophysectomized rat reveals the rather surprising fact that the hypophyseal hormones in normal amounts, so necessary for follicular growth, also depresses ovogenesis or the production of new germ cells.

Eight rats were hypophysectomized at varying times from twelve to ninety days before autopsy (see Table 1). The ovaries of these were serially sectioned and stained with uniform procedure for each. The ova and primordial follicles in the entire ovary were counted, with the few larger follicles and corpora that were present, a single ovary being used from each rat. The results of these counts are shown in the appended table.

After hypophysectomy the ovary of the rat rapidly shrinks to a small size. In the ovaries we have studied, from four to thirty corpora lutea were present, the remainder of the ovary being filled with interstitial tissue and primordial follicles and ova. The corpora are remarkably persistent structures in these ovaries. Smith[1] found that corpora one-half millimeter in diameter were still in evidence at nine and one-half months after the operation. Although, in our own rats, evidences of regressive changes have appeared in all of the corpora, yet the size undergoes relatively little diminution in the first fifty days following the operation. In rat 1130, the largest corpus was about one-half that of the early part of pregnancy.

TABLE 1.—*Ova and follicles in hypophysectomized rats.*

Rat	Days After Hypophysectomy	Ova and Primordial Follicles	Corpora	Total	Age
5976	12	2822	30	2852	117
5929	20	4311	23	4334	95
4343	35	4100	30	4130	123
1121	50	3927	4	3931	166
8643	50 right	4681	22	4703	
	64 left	4969	41	5010	
1141	62	4715	9	4724	186
1081	79	3605	17	3622	203
1130	90	4345	8	4351	202

Those that were pregnant at the time of the operation show slightly larger corpora than were present in the nonpregnant rats. The number decreases by the end of fifty days, those that persist being probably the last "crop" which ovulated.

Interstitial tissue increases with the gradual disappearance of the older corpora and large follicles in these ovaries, and, in most cases, shows degenerative changes in the nuclei. In addition to that formed from degenerating follicles and corpora, the germinal epithelium also adds to the supply by the formation of groups of cells which are indistinguishable from other interstitial cells after they have severed all connection with the epithelium. This is relatively rare and is the same process that occurs normally during both the pregnant and nonpregnant periods.

The production of new germ cells is abundant in the ovary of the hypophysectomized rat. When the number of these was counted, it was found that the amount of ovogenesis, as shown by the number of ova and primordial follicles, was greater than is found in the ovary during the normal oestrous cycle or in pregnancy, the number produced being from two to three times that found in the normal rat. These counts are shown in the table. The germinal epithelium shows active proliferation of single ova as well as epithelial cords from which ova are developed, processes similar in every respect to those found in the normal rat.[2]

In the small follicles, which may occasionally reach a fairly large size (270 microns in diameter in rat 1130 at day 90), with six or eight or even more rows of cells in the granulosa, growth, as shown by the number of mitoses in the cells of the granulosa, seems to be about as rapid as in the normal ovary. As many as a dozen or more mitotic figures may be seen in one section of a follicle 200 microns in diameter. These evidences of normal growth in small follicles, combined with the amount of active proliferation from the germinal epithelium, seem to establish the fact beyond doubt that the large number of ova and primordial follicles found in these ovaries is not an accumulation over long periods of time, but is the result of an actually greater rate of ovogenesis than occurs in the normal rat. This increase evidently begins a short time after hypophysectomy and seems to be due to the withdrawal of the hormones of the hypophysis.

The amount of atresia in the small follicles and ova also offers further evidence to establish this point. Very many ova degenerate before the primordial stage is reached, a few follicle cells only being present. Those that reach a larger size soon degenerate, resulting in the presence of much interstitial tissue. Mitotic division of the nuclei, even to the formation of typical polar bodies or of several larger cells, is frequent in these atretic follicles as in those of the normal rat. Such an amount of atresia would not take place if only the normal number of new germ cells were being formed, with a slow accumulation to produce the large number actually present.

In this group of rats four were pregnant at the time of operation, this occurring at the ninth and twelfth days of pregnancy. There were no differences, either in morphology or in the rate of ovogenesis, between these and the remainder of the group which were nonpregnant at the time of operation, except in the size of the corpora, the latter having the smaller corpora.

One ovary was removed from one rat at the fiftieth day after hypophysectomy and the remaining ovary secured at the sixty-fourth day. When the ova and primordial follicles were counted it was found that more ova were present at the latter date, but this probably represents only a normal variation.

A further discussion of the significance of these findings will be given in subsequent papers.

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CORONARY DISEASE—ITS PATHOGENESIS*

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DISCUSSION *by William H. Leake, M. D., Los Angeles; Donald J. Frick, M. D., Los Angeles; Eugene S. Kilgore, M. D., San Francisco.*

THIS contribution is concerned principally with the etiology and pathogenesis of lesions of the coronary arteries. It is based largely on a review of the records of 8,500 autopsies. Three groups of heart lesions have been segregated, first 114 cases of recent coronary occlusion, second 58 cases in which the heart showed evidence of healed infarction, and third, 135 cases of diffuse myocardial fibrosis without definite localized scarring.

OUTSTANDING FEATURE OF CORONARY DISEASE

The outstanding feature of coronary disease is the presence of arteriosclerosis (intimal atherosclerosis) involving greater or less portions of the coronary arteries with consequent lessening of the blood stream, and often associated with thrombosis resulting in complete obstruction. These disturbances profoundly influence the function and structure of the cardiac muscle. Other lesions such as syphilitic arteritis and embolism occur less frequently.

The importance of organic heart disease needs no emphasis. Of the recognized types of heart disease the group including the hypertensive disturbances and the coronary lesions is by far the largest. This group of heart cases is often said to have "chronic myocarditis." It would seem that from both the pathological and clinical viewpoint the use of this term should be discouraged and more accurate terminology used.

The American Heart Association[1] uses the term "arteriosclerotic heart disease," their definition appearing to lack in clarity and definiteness and seemingly including the concept of systemic arteriosclerosis as well as sclerosis of the vessels of the heart itself. From the standpoint of the pathologist it would seem preferable to confine the term to those hearts exhibiting localized atherosclerosis. It is recognized that coronary arteriosclerosis of high grade may occur without any marked sclerotic changes in other parts of the body; and, conversely, that generalized arteriosclerosis of high grade may exist without any serious involvement of the vessels of the heart. The series here studied supports this view.

CAUSATIVE FACTORS OF ARTERIOSCLEROTIC DISEASE

Assuming that the characteristic lesion of coronary heart disease is the sclerosis of these arteries, it is obvious that the essential causative factor is the underlying cause of arteriosclerotic disease, whatever that may be. Much has been written, but there is no general agreement among students of medicine as to its cause. Is it the pressure of the circulating blood? Is it some toxic agent, organic or inorganic? Is it an inherent defect of metabolism? It is quite generally recognized that we have no definite evidence incriminating lead, alcohol, tobacco, or bacterial toxins. We do know that often several members of the same family are victims of coronary disease, suggesting a hereditary tendency.

There are some facts which seem to support the contention that the intravascular tension is an essential factor. These include the fact that arteriosclerosis of the systemic circulation is almost universal in old age; but that normally the pulmonary arteries, with their lower blood pressure, are unaffected. On the other hand, in circulatory disturbances which result in abnormally high pressure in the pulmonary circulation, arteriosclerosis does occur in those arteries. In hypertensive disease arteriosclerosis occurs at a younger age than otherwise. These observations lead to the assumption that arteriosclerosis may result on the one hand from long-continued normal pressures or, on the other hand, occur more quickly in the presence of abnormally high pressures.

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